

MONOCLONAL ANTIBODIES THAT BIND OR NEUTRALIZE DENGUE VIRUS

Replacement Sheet

Lai et al.

Appl. No.: Unknown Atty Docket: NIH272.001NP

1/22

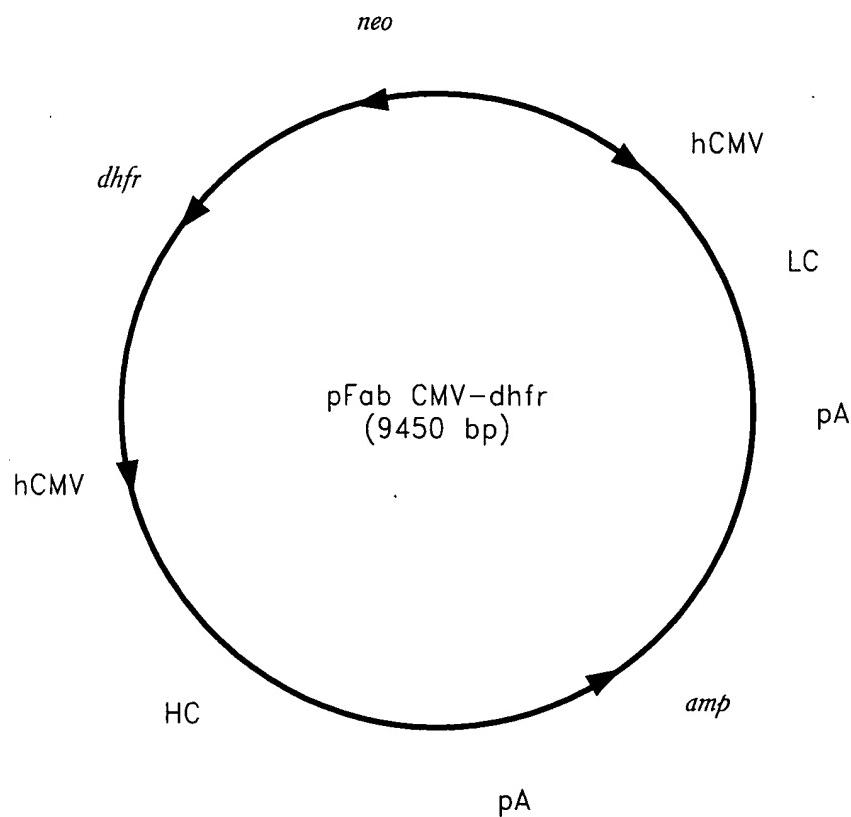


FIG. 1A

MONOCLONAL ANTIBODIES THAT BIND OR NEUTRALIZE DENCUE VIRUS

Replacement Sheet

Lai et al.

Appl. No.: Unknown Atty Docket: NIH272.001NP

2/22

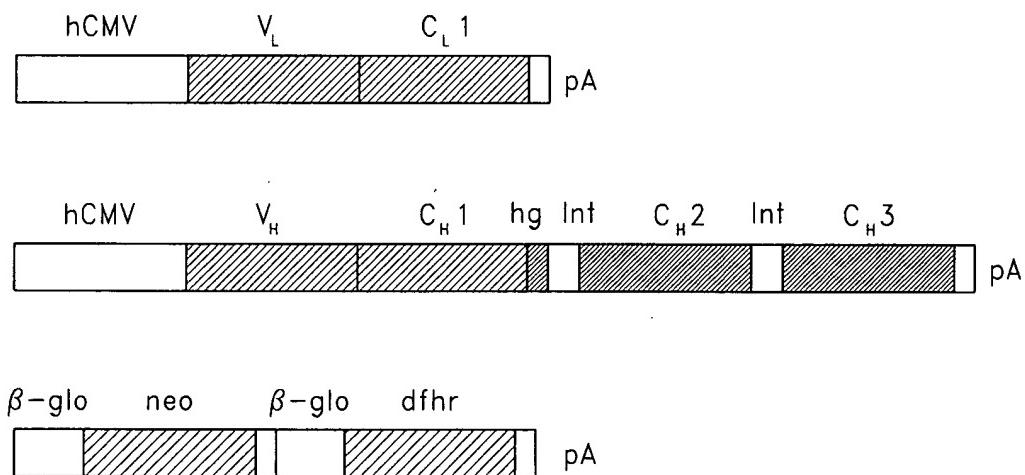


FIG. 1B

MONOCLONAL ANTIBODIES THAT BIND OR NEUTRALIZE DENGUE VIRUS

Replacement Sheet

Lai et al.

Appl. No.: Unknown Atty Docket: NIH272.001NP

3/22

(A)		FR1	CDR1	FR2	CDR2
5A7	--ELTQGPATLSSLSPGERATLSC	RAGQSLDS-----SLLS	WYQQKPGQAPRLIMY	DASTRAP	
3C1	ELQM,,S,,A,V,D,V,VT,	''SED,N-----KW,A	''''''K,'I,'	K,,SLES	
3E4	--,,S,LS,PVTL,QP,SI,'	,SS,N,VHSDGNTY,'	,I,,R,,P,,I,	KV,N,DS	
7G4	--,,S,,A,V,D,V,IT,	,,S,GIS-----,W,A	,,,'K,,KF,I,	K,,SLES	
5H2	ELQM,,S,SS,,A,V,D,V,IT,	,,S,DIS-----IR,N	,,,'K,,I,	,,,,LES	
5D9	--,,S,SS,,A,V,D,V,IT,	,,S,DIS-----NR,N	,,,'G,KF,,	,,,,SLVS	
		FR3	CDR3	FR4	
5A7	GVPARFSGSGSGTDFLTISLQPEDFAVYY	CQQHYNLPR	T	FGQGTTKLEIKRT	
3C1	,,,S,,,'E,,D,,,'	''''YQSY,Y,'	,'P,,,'		
3E4	,,,D,,,'A,,K,TRVEA,VGL,'	'V,GVQF,I,	,'P,,,'		
7G4	,,,S,,,'E,,D,,,'	,,YGSY,L,	,,P,,VD,,		
5H2	,,,S,,,'T,,'	,,FNSY,L,	,,G,,V,,		
5D9	,,,S,,,'	,,FNSY,L,	,,G,,V,,		

FIG. 2**FIG. 2A****FIG. 2B**

MONOCLONAL ANTIBODIES THAT BIND OR NEUTRALIZE DENGUE VIRUS

Replacement Sheet

Lai et al.

Appl. No.: Unknown Atty Docket: NIH272.001NP

4/22

(B)

	FR1	CDR1	FR2	CDR2
5A7	EVQLLES-GGGLVQPGGSLRLSCAASGVTF	SYWMH	WVRQAPGKGLEWV	SRINSDGSSTNYADSVEG
3C1	''''''-AEVKK, , , VKV, , , KV, , G, L,	GIS	'''''' Q, P, , M	GV, IPIRGTA, , , QKFQ,
3E4	''''''-QS, AEVKK, , , VKV, , , KV, , G, ,	RNPIS	'''''' Q, , , M	, V, VPIVGT, KH, QKEQ,
7G4	''''''-T, , , , , T, , , , F, ,	'''''	'''''' P, , ,	AL, KK, , , EKY, , E, , K,
5H2	''''''-P, , , K, SET, S, T, TV, , GSI,	DFYWS	, L, , S, , , , , I	GYAH, RV, -AY, NP, LKS
5D9	''''''-P, , , K, SET, S, T, TV, , GSI,	DFYWS	, L, , S, , , , , I	GVAH, RV, -AY, NP, LKS
	FR3	CDR3	FR4	
5A7	RFITISRDNAKNTLYLQMNSLRAEDTAVYYC	SRGGGLWDWSPRRIEETKTPFDY	WGQQGTLVTVSS	
3C1	, V, YTA, ESTS, V, MELS, , , S, , , ,	AT-----G, , GRYPTGS, , ,	, , , A, , , , ,	
3E4	, V, , TA, ESTS, A, MELS, , , S, , , ,	AT-----Y, , YADVSSYSE,	, , , , , , , ,	
7G4	, , , , , S, , , , , , , ,	T, ----- RITTLTVISDA, , I	, , , M, , , ,	
5H2	, V, , V, TS, , Q, S, RLSAVT, A, , , L, , ,	A, -----QGTGTTGVSED, F, L	, , , , K, I, , L	
5D9	, V, , V, TS, , Q, S, RLSAVT, A, A, L, , ,	A, -----QGTGTTGVSED, F, L,	, , , , K, I, , L,	

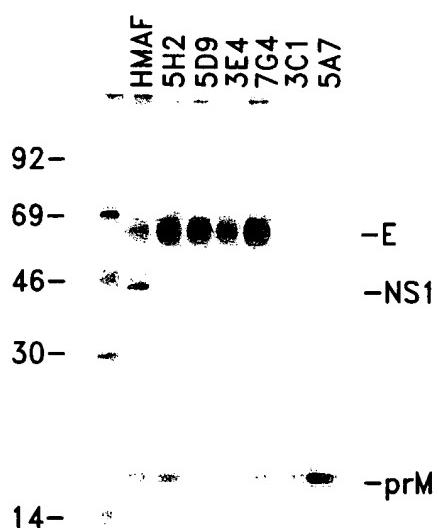
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Replacement Sheet

Lai et al.

Appl. No.: Unknown Atty Docket: NIH272.001NP

5/22



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FIG. 3A

6 / 22

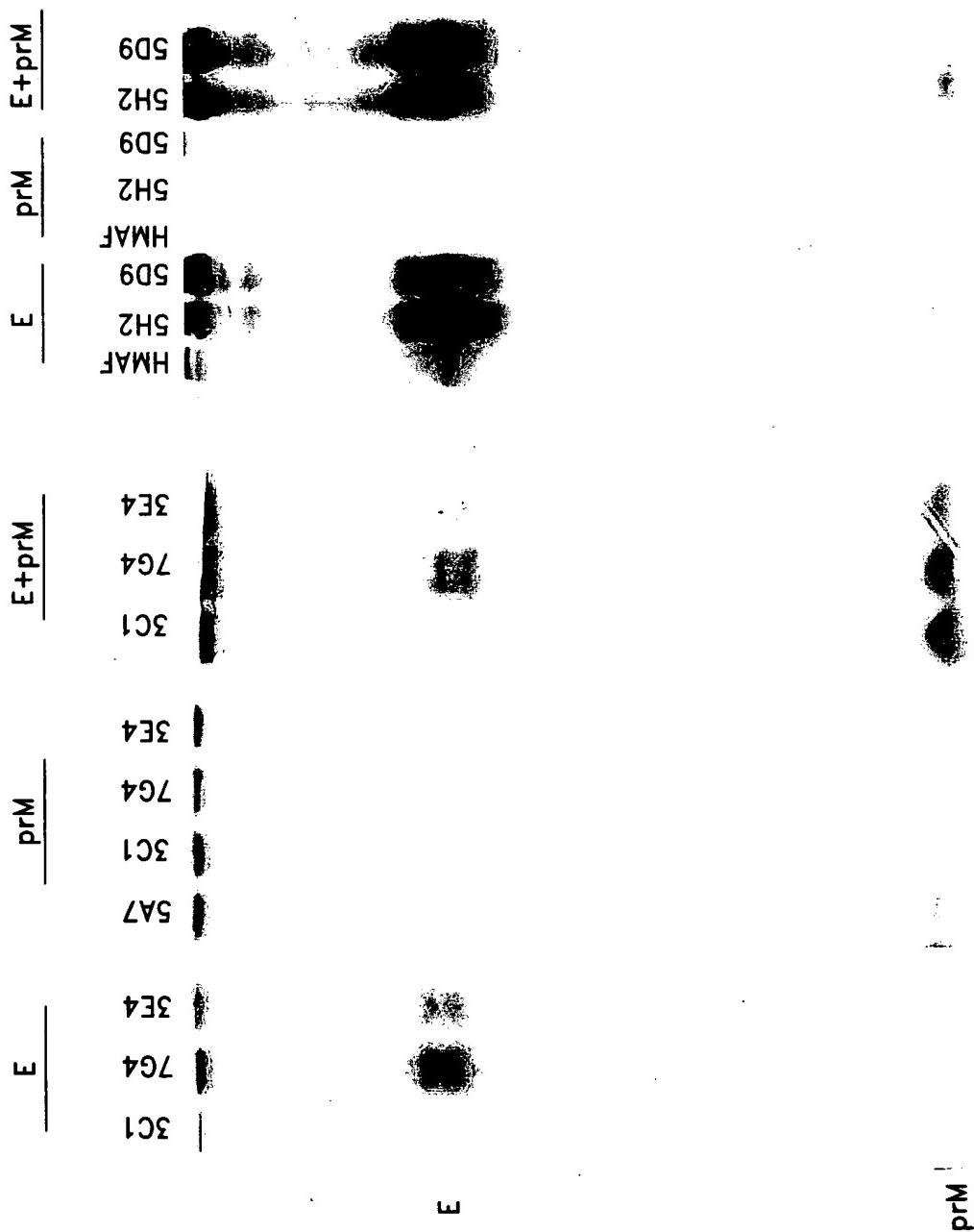
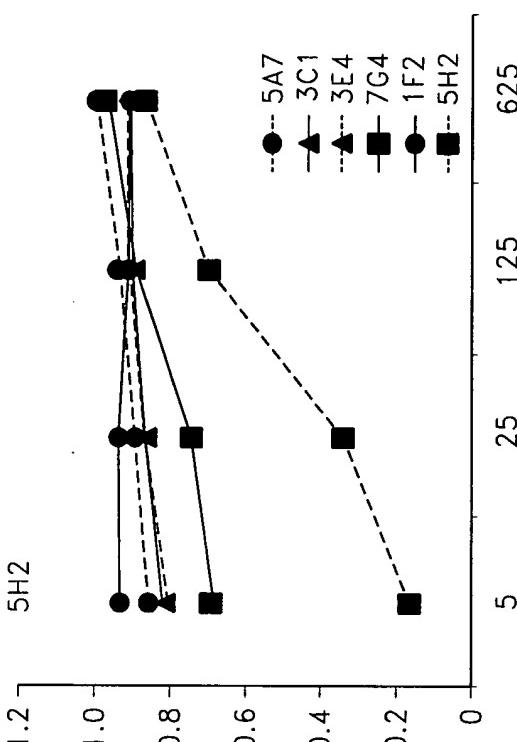
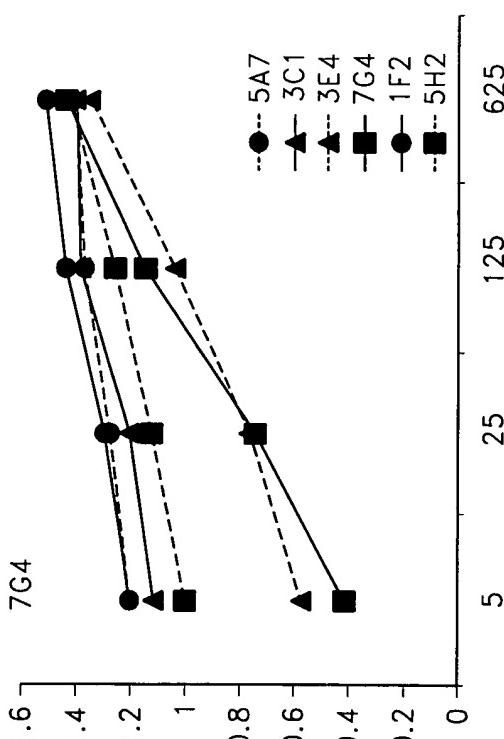
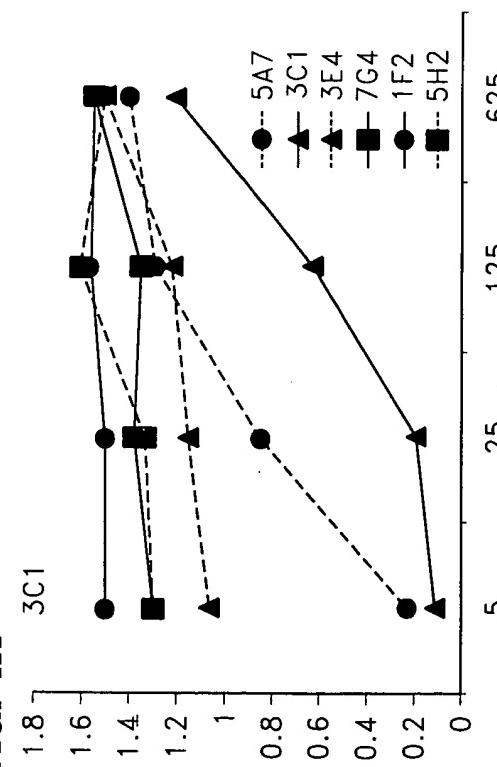


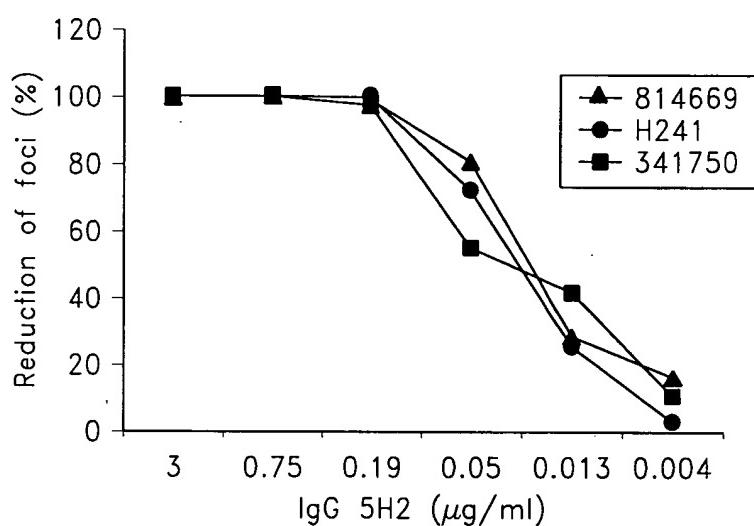
FIG. 3B

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7/22



8/22

**FIG. 5**

MONOCLONAL ANTIBODIES THAT BIND OR NEUTRALIZE DENGUE VIRUS

Replacement Sheet

Lai et al.

Appl. No.: Unknown Atty Docket: NIH272.001NP

9/22

	FR1	CDR1	FR2	CDR2
2H7	ELQMTQSPPSSLASAVGDRVTITC	RASQSQITIN-----	WYQQKPKAKPILLIS	YSSTTLQS
2H5	--EL.....V.....	T.....V.....	N.....Y	FA...H..
3A2	--EL.....V.....	T...A.....	Y HA....
1A5V.....	T...A.....	Y HA....
1B2	G SS-----E N	Y DA. S. E..
1A10	L...VAP.QPAS.S.	KS...LHSDGNT.F	L...S.QS.Q	Y GLSNRA.
3E4	A.L...L.PVTL.QPAS.S.	RS...NLVHSDGNT.S	IQ.RP.QP.R	Y KVSNRD.
	FR3	CDR3	FR4	
2H7	GVPSREFSGSGSGTISLQPEDFATYY	CHYG-YGTHT	FGPGBTKVDIKRT	
2H5N.....D.....	Q...-...Q..	..Q...LEV...	
3A2	I.....	D.....Q...	LE.....
1A5	I.....	D.....Q...	LE.....
1B2	QHFNSFPW.	Q...LE...	
1A10	D.....K..QVEA.VGVF.	MQ.TQLPY.	..Q...LE...	
3E4	D.....A.....K..TRVEA.VGLY.	VQ.VQFPI.	..Q...RLE...	

FIG. 6A**FIG. 6B**

MONOCLONAL ANTIBODIES THAT BIND OR NEUTRALIZE DENGUE VIRUS

Replacement Sheet

Lai et al.

Appl. No.: Unknown Atty Docket: NIH272.001NP

10/22

	FR1	FR2	CDR1	FR3	CDR3	FR4
2H7	EVQNLLE-SGGGLVQPGGSSRLSCAASGFTIS--	DNVNMH	WVRQAPGKGLEWV	ALIYSAD-STHYADSVKG		
2H5	-	--	.	.	.	-T-
3A2	Q.....	V.....	.	.	.	-T-
1A5	-	--	.	.	.	-T-
1B2	P...K.SQTLS.T.V..GSITSD	HYFWS	M..R..I	GY.SYRG-T.Y.NP.L.S		
1A10	E.AEVKK..SSVKV..KV..GTF.--	R.PIS	Q..M	GV.VPIVGT.KH.QKFQ.		
3E4	Q..AEVKK..SSVKV..KV..GTF.--	R.PIS	Q..M	GV.VPIVGT.KH.QKFQ.		
2H7	RETISRDNSKNTLYLQMDGLRPEDIAVYIC	AREYCTGGT-CFAHFDY	WGQGTLVTVSS			
2H5	.	S.....	D.-	.	S...	
3A2	.	S.....	G.....	.	T...	
1A5	.	S.....	D.-	.	S...	
1B2	.V.M.VTAA..	.	ASV.AGMPAAGTL.H			
1A10	RV.IIA.ESTSTAYMELSS..S..	.	TYYAD.----SSYSEY			
3E4	RV.IIA.ESTSTAYMELSS..S..	.	TYYADV.----SSYSEY			

FIG. 6B

MONOCLONAL ANTIBODIES THAT BIND OR NEUTRALIZE DENGUE VIRUS

Replacement Sheet

Lai et al.

Appl. No.: Unknown Atty Docket: NIH272.001NP

11/22

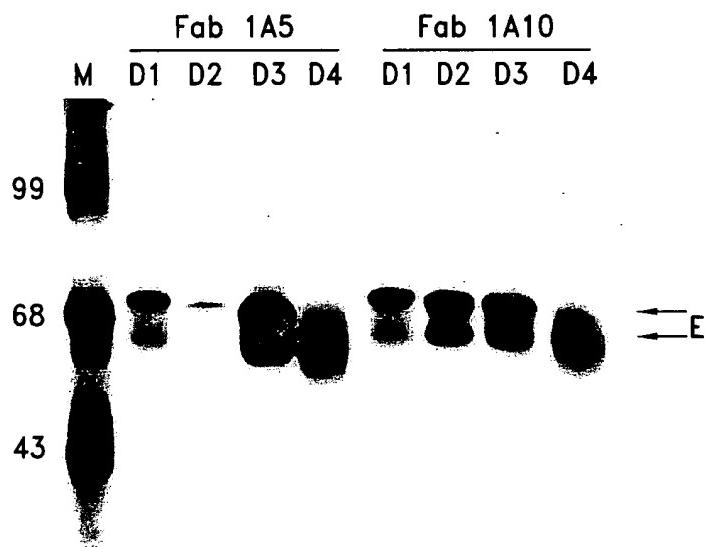
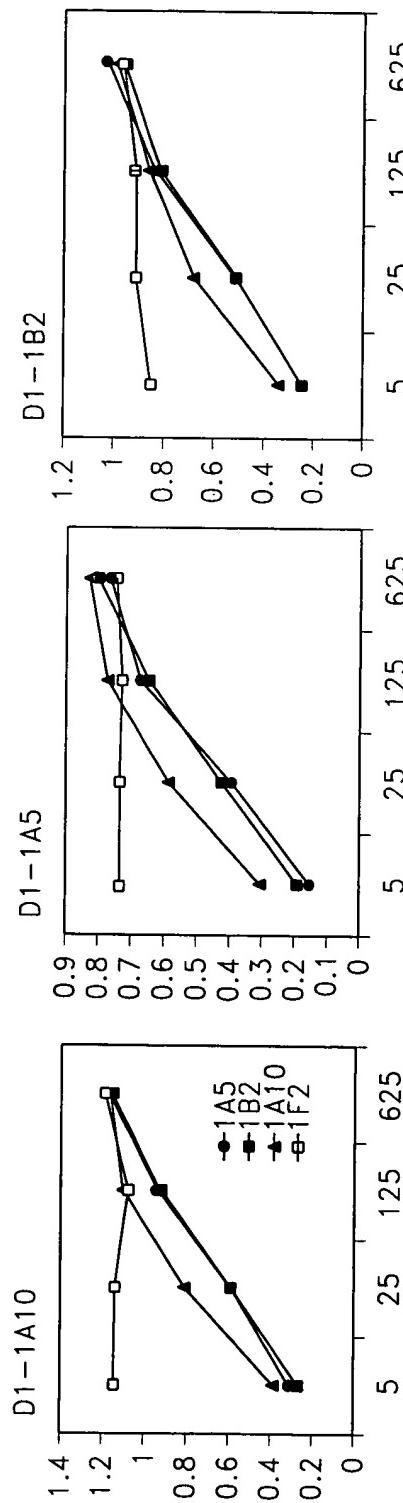
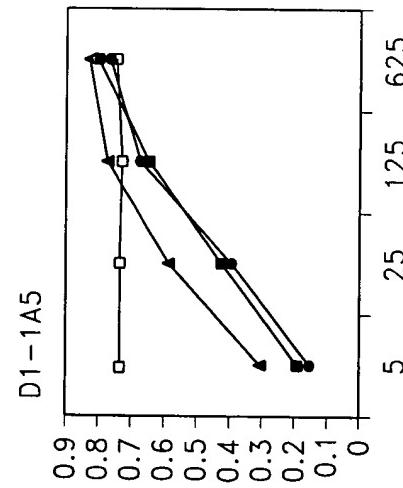
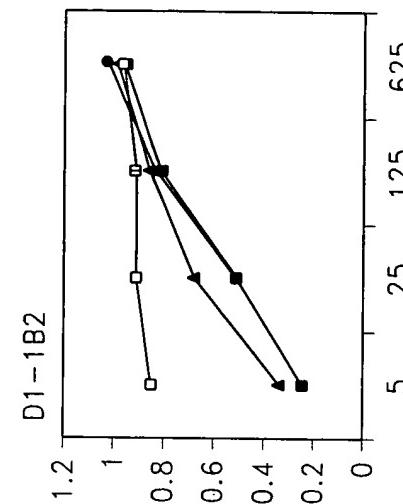
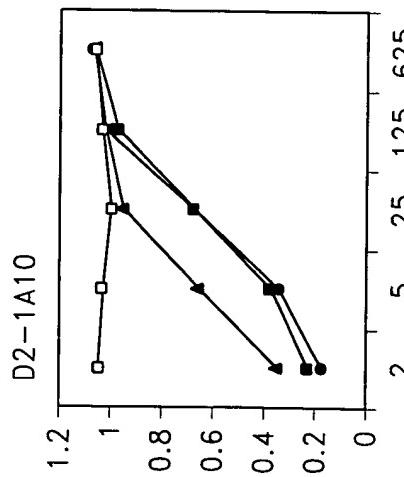
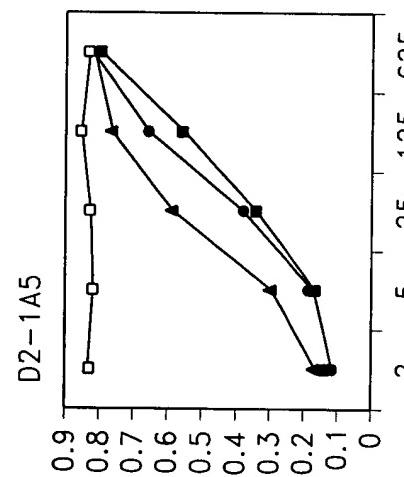
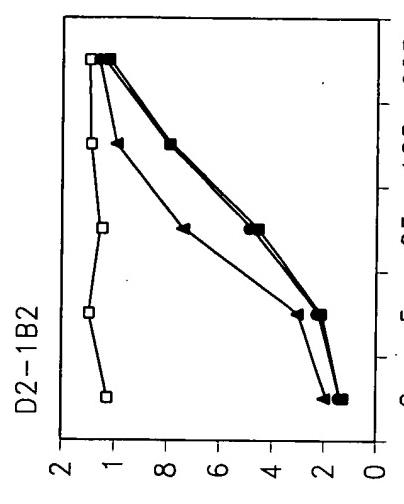


FIG. 7

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12/22

FIG. 8A**FIG. 8B****FIG. 8C****FIG. 8D****FIG. 8E****FIG. 8F**

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Replacement Sheet

Lai et al.

Appl. No.: Unknown Atty Docket: NIH272.001NP

13/22

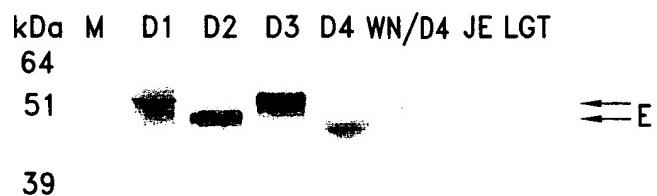


FIG. 9

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Replacement Sheet

Lai et al.

Appl. No.: Unknown Atty Docket: NIH272.001NP

14/22

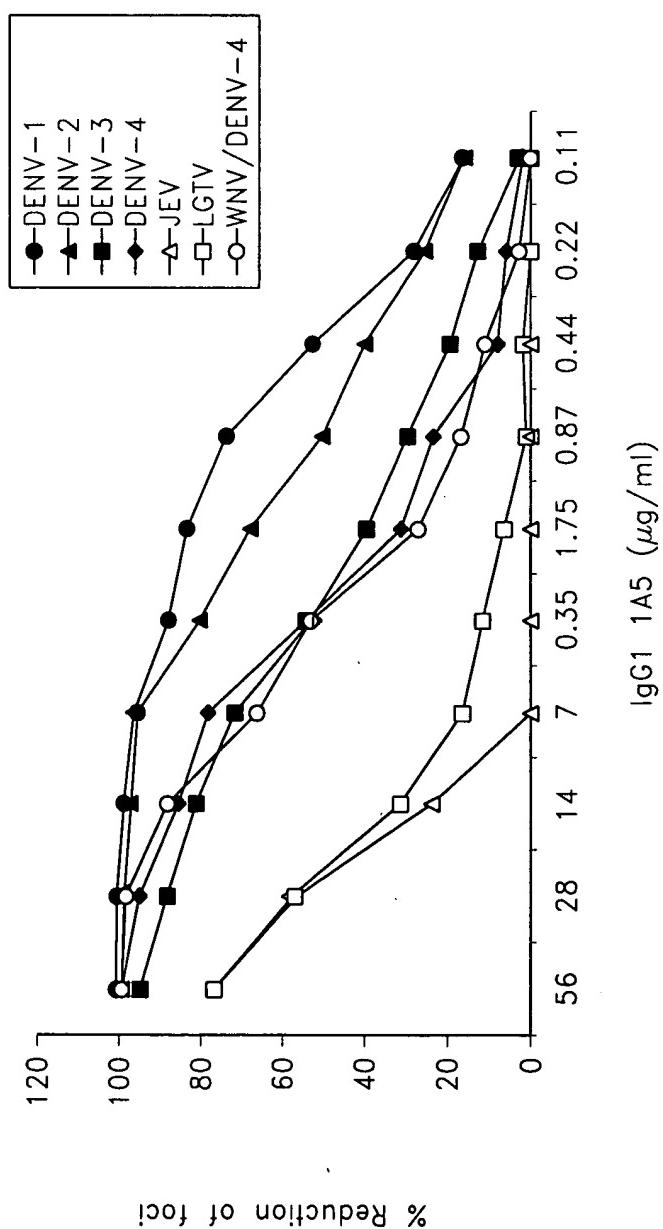
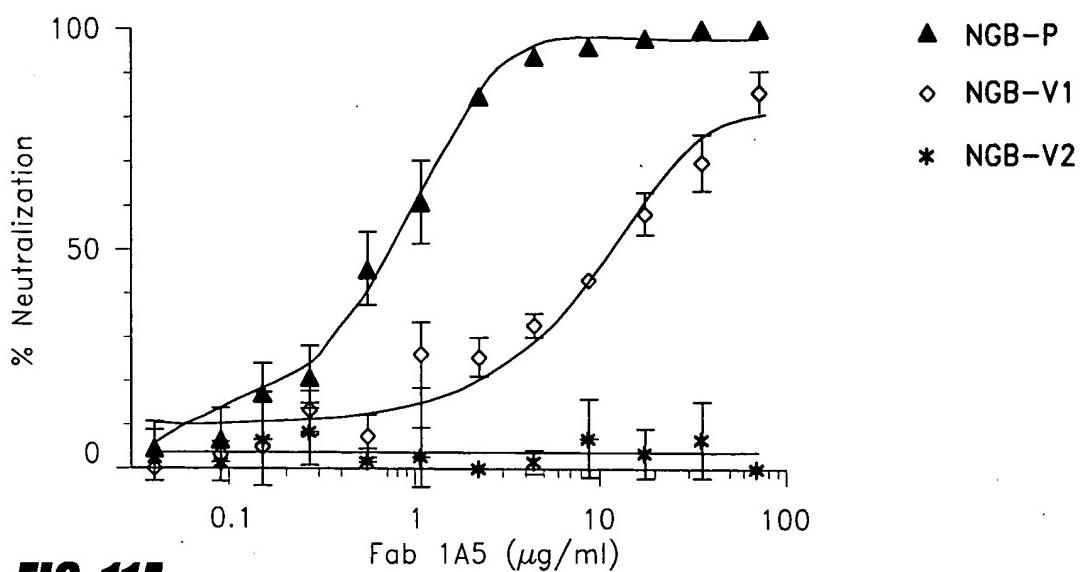
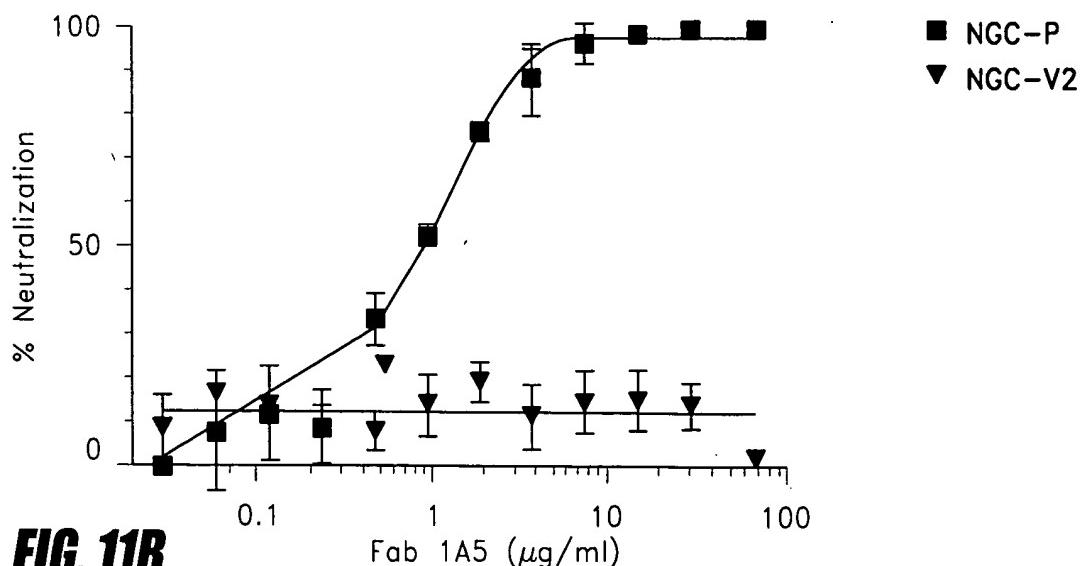


FIG. 10

15/22

**FIG. 11A****FIG. 11B**

MONOCLONAL ANTIBODIES THAT BIND OR NEUTRALIZE DENGUE VIRUS

Replacement Sheet

Lai et al.

Appl. No.: Unknown Atty Docket: NIH272.00INP

.16/22

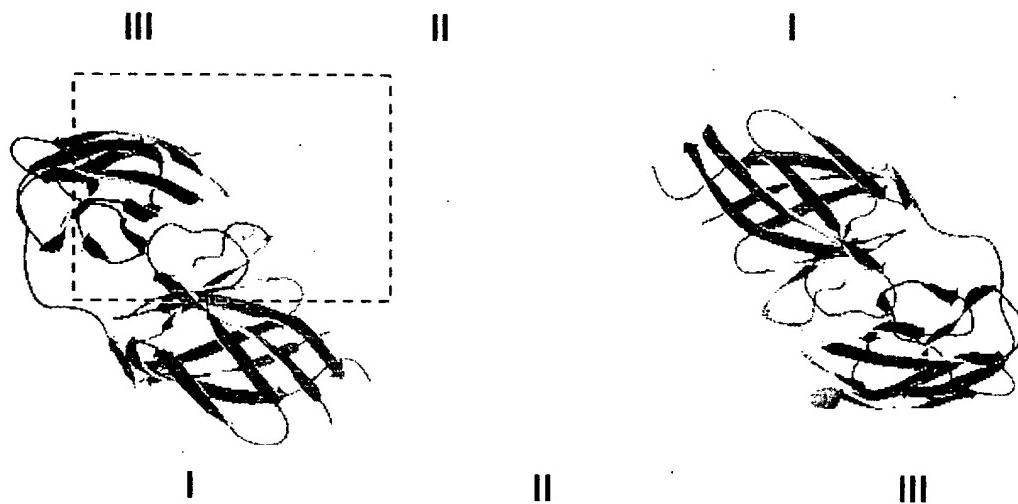
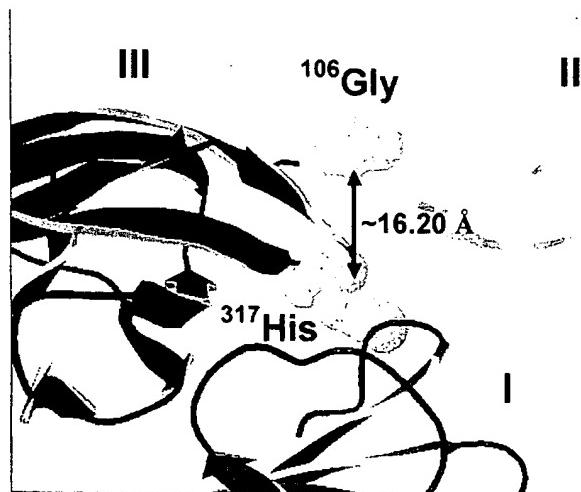
		C	Gly ₁₀₆	d
DENV-2 P	89	RFVCKHSMV <u>DRGWGN</u> GCLFGKGGIVTCAMFT		120
DENV-2 V1		-----		
DENV-2 V2		-----V-----		
DENV-1		N---RRTF-----	SLI---K-K	
DENV-3		NY---TY-----	SL---K-Q	
DENV-4		QYI---RRDV-----	V---K-S	
WNV		A---RQGV-----	S-D---K-A	
JEV		SY---QGFT-----	S-D---K-S	
JEV SA14-14-2		SY---QGFT-----	F---S-D---K-S	
SLEV		T---RDV-----	S-D---K--	
YFV Asibi		DNA---RTYS-----	S---A---K--	
YFV 17D		DNA---RTYS-----	S---A---K--	
LGTV		GT---RDQS-----	H-----S---VK--	
TBEV		GT---RDQS-----	H-----S---A-VKAA	

FIG. 12A

			A	His ₃₁₇	B	
DENV-2	P	306	FKVVKEIAET <u>Q</u> HGTIVIRVQY			326
DENV-2	V1		-----Q-----			
DENV-2	V2		-----			
DENV-1			--LE--V-----		VLVQ-K-	
DENV-3			-VLK--VS-----		L-K-E-	
DENV-4			-SID--M-----		T-VK-K-	
WNV			--FLGTP-D-G---		V-LEL--	
JEV			-SFA-NP-D-G---		V--ELT-	
JEV SA14-14-2			-SFA-NP-D-G---		V--ELT-	
SLEV			-TFS-NPTD-G---		VIVEL--	
YFV Asibi			MFF--NPDT-G---		V-MQ-KV	
YFV 17D			MFF--NPDT-G---		V-MQ-KV	
LGTV			-TWKRAPTD SG-D-V-ME-GF			
TBEV			-TWRRAPTD SG-D-V-ME-TF			

FIG. 12B

17/22

**FIG. 13A****FIG. 13B****BEST AVAILABLE COPY**

MONOCLONAL ANTIBODIES THAT BIND OR NEUTRALIZE DENGUE VIRUS

Replacement Sheet

Lai et al.

Appl. No.: Unknown Atty Docket: NIH272.001NP

18/22

Mab 3H5

kDa	M	1	2	3	4	5	6
64							
51							
39							

Fab 1A5

kDa	M	1	2	3	4	5	6
64							
51							
39							

FIG. 14A

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19/22

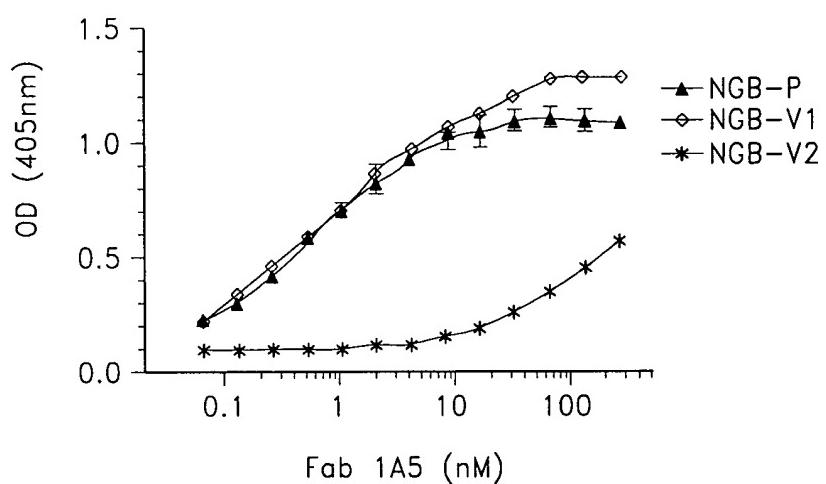
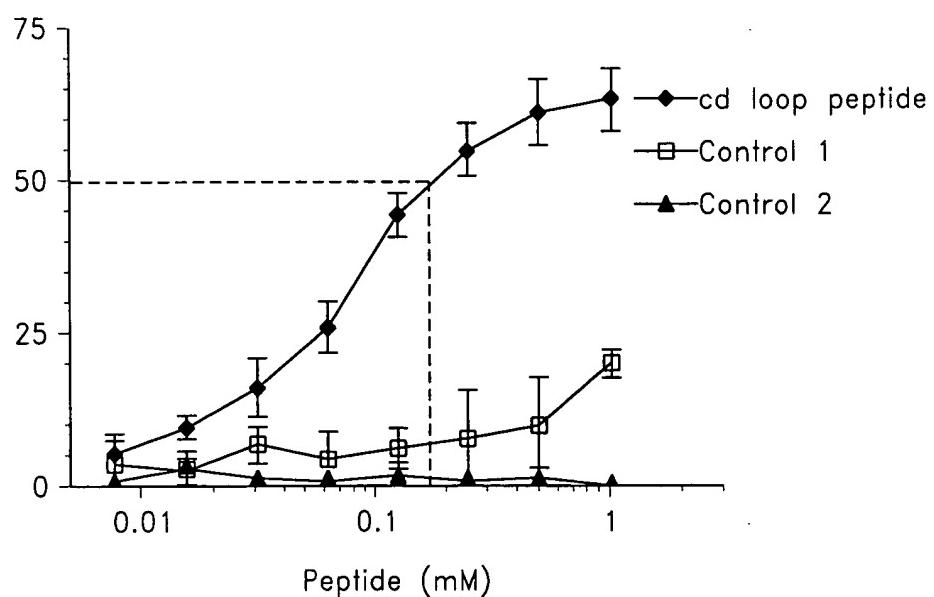
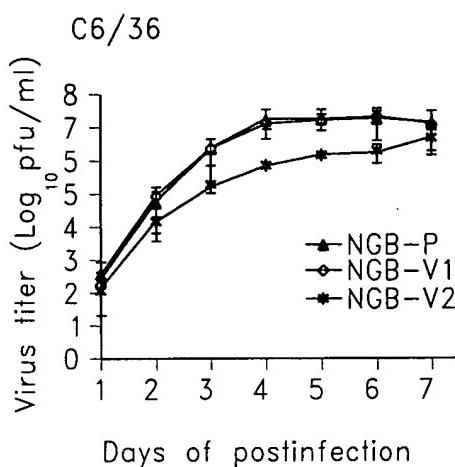
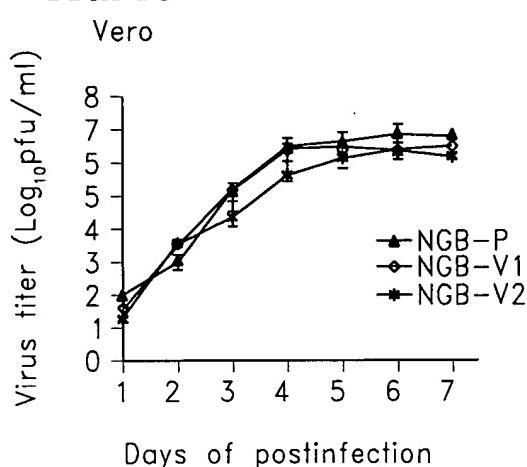
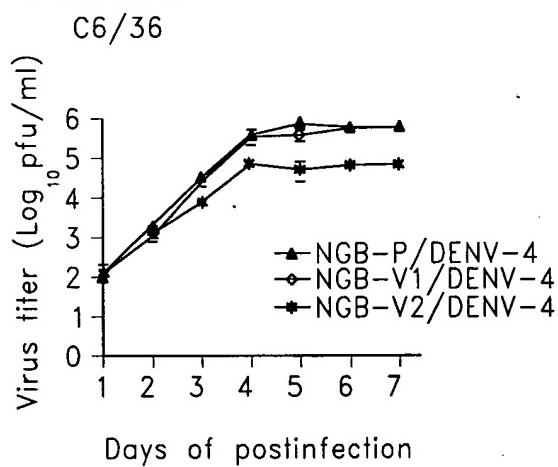
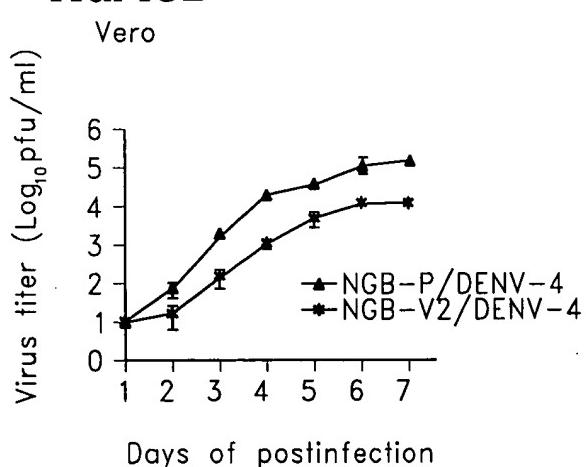
**FIG. 14B****FIG. 15**

FIG. 16A**FIG. 16B****FIG. 16C****FIG. 16D**

MONOCLONAL ANTIBODIES THAT BIND OR NEUTRALIZE DENGUE VIRUS

Replacement Sheet

Lai et al.

Appl. No.: Unknown Atty Docket: NIH272.001NP

21/22

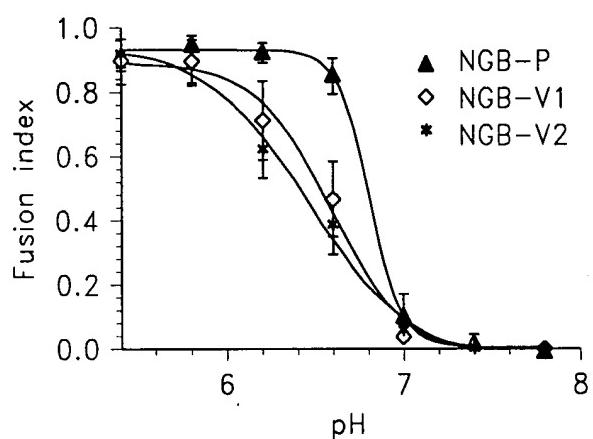
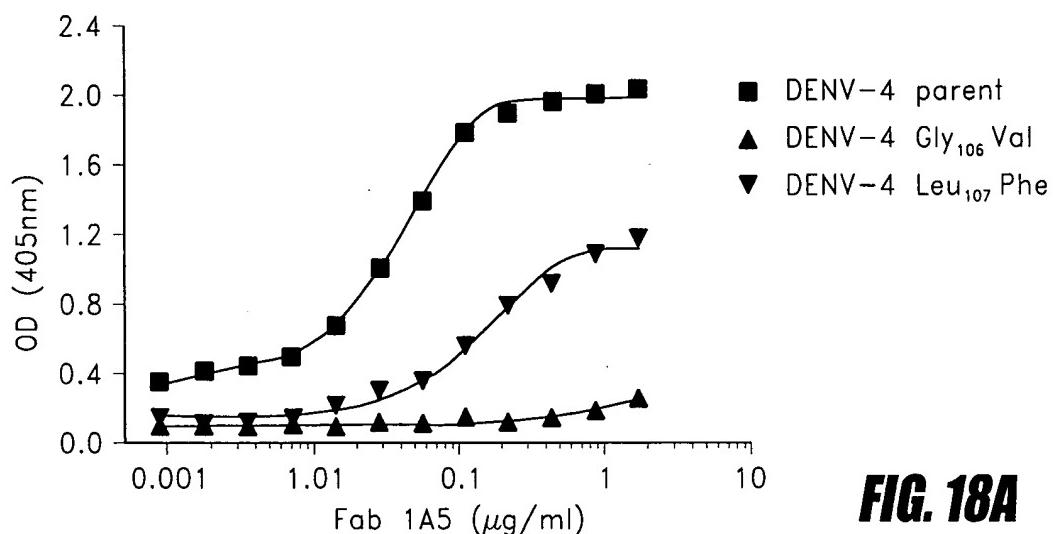
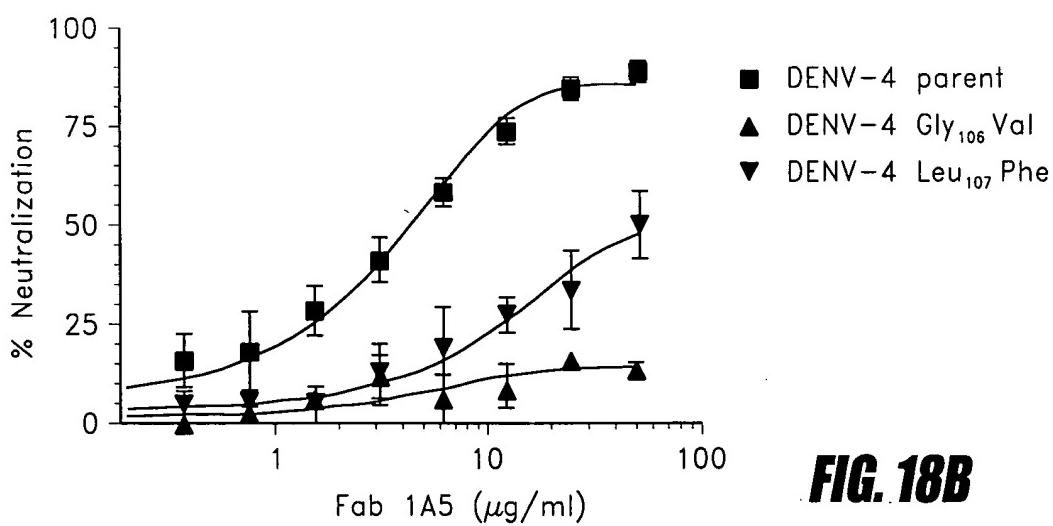


FIG. 17

22/22

**FIG. 18A****FIG. 18B**